REMARKS

The Office Action set forth the following rejections:

Claims 1-23 and 26-28 were rejected under 35 U.S.C. §112, second paragraph, as indefinite on various grounds;

Claims 1-23 and 26-28 were rejected under 35 U.S.C. §112, first paragraph, as only being enabled for Q as pyridyl and pyrimidyl, Ar as phenyl and R_2 as alkyl and claims 26-28 are not enabled for treating "any CNS disorder or kidney disorder";

Claims 1 and 11 were rejected under 35 U.S.C. §102(b) as being anticipated by Interchim Intermediates; and

Claims 1-3, 10, 11, 23 and 27 were rejected under 35 U.S.C.§102(e) as being anticipated by WO 2004/058265A to Jones.

Applicants have cancelled claims 26 and 28 and amended claims 1, 3, 5, 8-14, 18-20, 23 and 27 by this Amendment.

With respect to the 35 U.S.C. §112, second paragraph, rejection we have made the following amendments:

In claim 1, we have restricted Q to pyridindiyl and pyrimidindiyl and Ar to phenyl, pyridyl and pyrimidinyl. Moreover, we have specified that Ar must be substituted by one or two radicals R^b. In the definition of R^b, we have deleted NH_2.

Claims 5, 8, 9, 13 and 14 have been amended to reflect the restricted definition of Q and to avoid redundancies.

Claim 8 has been amended to depend from claim 5. This is the correction of an obvious error, since, if claim 8 depended on claim 6, it would not be necessary to include the formula of Q. Furthermore, claim 9 would be superfluous since it would not

contain any limitation to claim 8 depending from claim 6. Thus, it is evident that claim 8 is intended to depend from claim 5.

In claims 10, 18 and 23, the objected term "where appropriate" has been replaced by "optionally".

In claims 12 and 20, the expression "R^1 is different from hydrogen and methyl" has been replaced by "R^1 is not hydrogen or methyl", as suggested by the Examiner.

In method claim 27, the functional definition has been replaced by a list of specific diseases or disturbances. Accordingly, claims 26 and 28 have been cancelled.

As to the objection of claim 19 as being improperly dependent from claim 13, the definition of Ar being phenyl is included in claim 13, when X and Y are both CH or one of X and Y is CH and the other is C-R^b.

It is submitted that the amendments and arguments set forth above are sufficient to overcome the rejections under 35 USC 112, second paragraph, and withdrawal of this rejection is requested.

With respect to the enablement rejection, submitted herewith is a declaration wherein the synthesis and the biological test data of further compounds which fall under the scope of claim 1 are presented. These data provide, for example, support for compounds, wherein R^1 and R^2 together form an alkylene group; for compounds, wherein two residues R^a is NR^6R^7, CN or halogen; and for compounds, wherein R^b is haloalkoxy.

As to Ar being pyridyl or pyrimidinyl, additional data will be presented if so requested.

In order to show that the present application is enabling as regards the synthesis of compounds wherein Ar is a heterocyclic residue, we enclose an internet search (www.emolecules.com) as Exhibit A wherefrom it can be seen that pyridyl sulfonyl chlorides and pyrimidyl sulfonyl chlorides having various kinds of substituents which fall under the scope of present claim 1 are commercially available. These sulfonyl cholorides can be used in the general method for the preparation of compounds I which is described in the present application.

We further enclose a search (www.emolecules.com, SciFinder and ACDFinder) as Exhibit B wherefrom it can be seen that bridged and condensed piparazines which can be used in the general method for the preparation of compounds described in the present application are also commercially available.

As to the definition of radicals of the compound of formula I which are not supported by specific examples in the specification or in the enclosed declaration, it should be noted that most of these radicals are chemically and biologically equivalent to radicals having meanings supported by the test data.

For instance, compounds wherein R is NR^3, wherein R^3 is C_1-C_4-alkyl, can be expected to have a similar biological effect as compared to the same compounds wherein R is NH.

Compounds wherein R^a is NH_2 or NHR^6 can be expected to have a biological effect comparable to that of compounds wherein R^a is NR^6R^7.

Since the positive effect of compounds I with R^a being C_1-C_4-alkyl or halogen has been proven in the test examples, it is clear that the same compound wherein R^a is C_1-

C_4-haloalkyl can be expected to have a comparable biological effect since this residue combines the properties of alkyl and halogen.

The same considerations apply to varying resides R^b. Since compounds wherein R^b is C_1-C_6-alkyl, C_1-C_6-haloalkyl or C_1-C_6-haloalkoxy have the desired biological effect, one can expect the same effect for compounds wherein R^b is C_1-C_6-alkoxy, since this residue combines the properties of alkyl and haloalkoxy. As the test data show, using a halogenated alkyl residue instead of a halogen-free alkyl residue R^b apparently has no dramatic effect on the biological activity of the compound. Thus, it can be expected that using a non-halogenated alkoxy substituent instead of a halogenated alkoxy group R^b will not change the biological activity of the compound.

The same thoughts apply to R^b being C_3-C_6-cycloalkyl-C_1-C_4-alkyl: Since compounds having C_3-C_6-cycloalkyl groups or C_1-C_4-alkyl groups have proven to be useful dopamine D_3 ligands, the same can be expected for compounds wherein R^b is C_3-C_6-cycloalkyl- C_1-C_4-alkyl, which represents a combination of the two former named groups.

The same applies to compounds wherein R^b is NHR^6, since it has been shown that compounds wherein R^b is NR^6R^7 show a good biological activity.

Since cyano groups and halogen residues are considered to be bioisosters, it can be expected that compounds wherein R^b is CN also exhibit the desired biological activity.

In order to overcome the enablement rejection of claim 27, we include the following documents that are attached as Exhibit C and are directed to the treatment of many of the specified diseases by D_3 receptor ligands:

- J.N. Joyce, Pharmacology and Therapeutics 90, 2001, 231-259 (see abstract and page 251, where it is said that D_3 receptor ligands can be expected to be effective in the treatment of schizophrenia, drug abuse, depression, amotivation....(see page 251, col. 2, chapter "7. Conclusions")
- J.N. Joyce et al., DDT vol. 10, number 13, July 2005, where it is said that D_3 receptor antagonists can be useful antipsychotic agents and may be used to treat cognitive symptoms and drug abuse. Although this document was published after the filing date of the present application, from the cited references, it can be seen that D_3 receptor ligands were known earlier to act as described in this paper (for drug abuse, see for example citations nos. 83, 84, 85, 86, 28 and 30 (compare page 923, col. 2, chapter "D_3 receptor antagonists in the treatment of drug abuse"). As to the usefulness of dopamine D_3 receptor ligands as antipsychotic and antiparkinsonian drugs, see for example citation 4).
- J. Laszy et al., Phsychopharmacology, 2005, 179, 567-575, where it is said that dopamine D_3 receptor antagonists possess cognition-enhancing activity which may be useful for the treatment of cognitive dysfunction. Although this document was published after the filing date of the present application, from the cited references (see especially page 567, col. 2, last paragraph to page 568, col. 1, first paragraph), the context between D_3 receptor ligands and cognitive activity was known much earlier.
- C.A. Heidbreder, Brain Research Reviews 49, 2005, 77-105, where it is said that dopamine D_3 receptor antagonists may be useful for treating

drug dependence and addiction. Although this document was published after the filing date of the present application, from the cited references (see especially page 79, col. 1, 2nd paragraph; in particular reference to citation 231), the context between D_3 receptor ligands and addiction was known much earlier.

- Z. Rogoz et al., Polish Journal of Pharmacology, 2003, 55, 449-454, where it is said that dopamine D_3 receptor agonists may play a role in the therapy of anxiety (see abstract).
- B. Mühlbauer, E. Küster, G. Luippold, Dopamine D_3 receptors in the rat kidney: role in physiology and pathophysiology, Acta Physiologica Scandinavica, 2000, 168 (1), 219-223, where it is said that D_3 receptors are implicated in the regulation of renal function. Unfortunately, we do not have a copy of this document, but can provide it, if required by the Examiner. The abstract reads as follows: *It is well accepted that Dopamine receptors play an important role in the regulation of cardiovascular and kidney function. Most of the knowledge on the renal actions of dopamine has been accumulated focusing on the prototypes of the two known dopamine receptor sub-families, i.e. D_1 and D_2. The dopamine D_3 receptor is a member of D_2-like sub-family and has been intensively studied in the neurosciences. Recently, the peripheral actions of this receptor sub-type have also raised considerable interest as well, because its effects on kidney function appear to be different from that of the other dopamine receptors. This short overview will summarize the*

data reported and add new results on the role of D_3 receptors in the regulation of renal function as well as their potential pathophysiological implications."

- S.C. Benoit, J.A. McQuade, D.J. Clegg, M. Xu, P.A. Rushing, S.C. Woods, R.J. Seeley, J. Randy, Altered feeding responses in mice with targeted disruption of the dopamine D_3 receptor gene, Behavioral Neuroscience, 2003, 117(1), 46-54, where the context of food intake and dopamine D_3-receptor ligands is shown. Unfortunately, we do not have a copy of this document, neither, but we can provide one, if required by the Examiner. The abstract is worded as follows: *"Dopamine signaling has been implicated in the control of food intake and body weight. In particular, dopamine is important in the control of meal size and number and is thought to mediate the response to metabolic deprivation states. In the present experiments, the authors assessed the role of the dopamine-3 receptor (D3R) in the feeding responses to 2-deoxy-D-glucose, mercaptoacetate, and peripheral insulin. All 3 compounds increased food intake in wild-type mice, but the hyperphagic responses were blunted in D3R-/-mice. In other experiments, D3R-/-mice were hyperresponsive to the administration of amylin and leptin relative to wild-type mice. These results support the hypothesis that D3Rs chronically inhibit the effects of adiposity hormones, thereby contributing to a net anabolic state."*

For the above noted reasons, withdrawal of the enablement rejection under 35 U.S.C. §112, first paragraph, is requested.

The Examiner further requested us to provide the time the compound disclaimed in claim 1 was first available for sale. Applicants inquired at Ambinter, Paris, but couldn't get any detailed information. It was only known that the compounds had been sold for several years. The disclaimed compounds form part of a substance library and are sold to enterprises/universities/research centers interested in testing a series of different compounds. Thus, it is difficult to tell how they are used and what types of activity they show. Applicant is not aware of any published information in this regard.

As to the requested information to the activity and/or uses for the compounds listed in the CHEMCATS Database cited in the IDS of January 24, 2005, Applicants are not aware of any such data, since these compounds are sold as building blocks for organic synthesis.

With respect to the novelty rejections under 35 U.S.C. §102, we have amended the claims to require Ar to be substituted by one or two groups R^b. Furthermore, in the definition of R^b, NH_2 has been deleted. Consequently, the claimed subject-matter is no longer anticipated by the cited Interchim reference.

With respect to the Section 102 rejection over Jones et al., a certified English Translation of the parent provisional application was submitted to the USPTO on September 9, 2003 and received by the USPTO on September 12, 2003. A copy of the date stamped postcard acknowledging receipt is enclosed as Exhibit D.

Accordingly, the Section 102 rejections should be withdrawn.

Favorable consideration and allowance of claims 1-23 and 27 is respectfully requested.

Respectfully submitted,

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